

IN THE CLAIMS

Please amend the claims as follows:

1. (AMENDED) A method for diagnosis of blood brain barrier permeability in a subject comprising:

detecting levels of S100 β protein in a blood sample derived from the subject prior to manifestation of neuronal damage in the subject; and

comparing the levels of S100 β protein detected in the sample to a level of S100 β protein in a control, wherein an increase in the level of S100 β protein detected in the sample as compared to the control sample is indicative of blood brain barrier permeability.

2. (Original) The method of claim 1, wherein the sample is scored based upon permeability of the blood brain barrier.

3. (Original) The method of claim 1, wherein the S100 β protein is detected using an immunoassay.

4. (Original) The method of claim 3, wherein the immunoassay is an immunoprecipitation assay.

5. (Original) The method of claim 1, wherein the levels of S100 β protein in blood samples over time indicates stages of diseased states.

6. (Original) The method of claim 1, wherein the indication of blood brain permeability is made independent of indicators of neuronal distress.

7. (AMENDED) The method of claim 1, further including ~~detecting levels of markers of neuronal distress, said markers being selected from the group consisting of NSE, GFAP, and elevated levels of S100 β protein beyond increased levels of S100 β~~ the step of monitoring markers of neuronal distress.

Claims 8-21 were cancelled.

22. (NEW) The method of claim 7, wherein said markers are selected from the group consisting of NSE, GFAP, and a second elevated level of S100 β protein.

23. (NEW) The method of claim 1, wherein said manifestation of neuronal damage are physical symptoms of neuronal damage.

24. (NEW) The method of claim 1, wherein said manifestation of neuronal damage is indicated by release of markers of neuronal damage into blood of the subject.

25. (NEW) The method of claim 1, wherein said control sample is a blood sample derived from the subject at a previous point in time.

26. (NEW) The method of claim 1, further including the step of comparing levels of S100 β to specific threshold values of S100 β protein to determine the presence of statistically significant concentrations thereof above normal levels.

27. (NEW) A method for diagnosis of blood brain barrier permeability in a subject, said subject being free of neuronal damage, said method comprising:

detecting levels of S100 β protein in a blood sample derived from a subject; and
comparing the level of S100 β protein detected in the sample to a level of S100 β protein in a control, wherein an increase in the level of S100 β protein detected in the sample as compared to the control sample is indicative of blood brain barrier permeability.

28. (NEW) The method of claim 27, wherein the sample is scored based upon permeability of the blood brain barrier.

29. (NEW) The method of claim 27, wherein the levels of S100 β protein in blood samples over time indicates stages of diseased states.

30. (NEW) The method of claim 27, further including the step of monitoring levels of markers of neuronal distress when increased levels of S100 β are detected.

31. (NEW) The method of claim 30, wherein said markers are selected from the group consisting of NSE, GFAP, and elevated levels of S100 β protein beyond increased levels of S100 β .

32. (NEW) The method of claim 27, wherein a statistically relevant first elevated level of S100 β is indicative of BBB in opening and the presence of both the first and a second elevated level is indicative of blood brain barrier opening and neuronal damage when said second elevated level is greater than said first elevated level.

33. (NEW) A method for diagnosis of blood brain barrier permeability in a subject comprising:

detecting levels of S100 β protein in a blood sample derived from a subject, said subject being predisposed to brain damage but free of symptoms of brain damage at the time of diagnosis; and

comparing the level of S100 β protein detected in the sample to a level of S100 β protein in a control, wherein an increase in the level of S100 β protein detected in the sample as compared to the control sample is indicative of blood brain barrier permeability.

34. (NEW) The method of claim 32, wherein the levels of S100 β protein in blood samples over time indicate stages of diseased states.

35. (NEW) The method of claim 33, wherein the sample is scored based upon permeability of the blood brain barrier.

36. (NEW) A method for diagnosis of blood brain barrier permeability in a subject comprising:

detecting a first elevated level of S100 β in the blood of a patient;

identifying a second elevated level of S100 β in the blood of the patient; and

comparing first and second elevated levels of S100 β wherein a statistically relevant first level of S100 β protein is indicative of blood brain barrier permeability without neuronal damage.

37. (NEW) The method of claim 36, wherein the second elevated level of S100 β has a value which is greater than said value of first elevated level of S100 β .

38. (NEW) The method of claim 36, wherein said value of said second elevated level of S100 β is indicative of neuronal damage.

39. (NEW) The method of claim 36, further including monitoring levels of markers of neuronal distress upon detection of said first elevated levels of S100 β .

40. (NEW) The method of claim 39, wherein said markers of neuronal damage are selected from the group consisting of NSE, GFAP, and elevated levels of S100 β protein beyond increased levels of S100 β .

41. (NEW) The method of claim 36, wherein said value of said second elevated level of S100 β is greater than twice the value of said first elevated level of S100 β .

42. (NEW) The method of claim 36, wherein said value of said first elevated level of S100 β is in the range of about 0.12 ng/ml to 0.35 ng/ml.

43. (NEW) The method of claim 36, wherein said value of said second elevated level of S100 β is in the range of about 0.35 ng/ml.